FPIN's Clinical Inquiries

A1C Testing in the Diagnosis of Diabetes Mellitus

Clinical Question

Can A1C measurements be used to diagnose diabetes mellitus?

Evidence-Based Answer

A1C testing is highly specific compared with a two-hour oral glucose tolerance test (OGTT) or a fasting plasma glucose test. However, because A1C testing is not sensitive enough to rule out diabetes if levels are normal, the test should not be used for diagnosing diabetes.1 (Strength of recommendation: C).

Evidence Summary

The accuracy of A1C testing for the diagnosis of diabetes was first evaluated using pre-1997 World Health Organization (WHO) criteria for a diabetes diagnosis (i.e., OGTT result more than 140 mg per dL [7.8 mmol per L] fasting or more than 200 mg per dL [11.1 mmol per L] at two hours). A meta-analysis1 (including 10 studies that evaluated A1C levels of 8,984 patients) that used a cutoff (i.e., upper limit of normal) A1C level of 6.3 percent (two standard deviations [SD] above the mean) showed that A1C testing was 66 percent sensitive and 98 percent specific for diagnosing diabetes (Table 11,2). Based on an assumed diabetes prevalence rate of 6 percent in the general population (i.e., persons without known diabetes), 63 percent of patients with an A1C level more than 6.3 percent would have diabetes (positive predictive value [PPV] = 63 percent).

table 1

Accuracy of AIC Testing for Diabetes			
Cutoff A1C level (%) (standard deviations above the mean)	Sensitivity (%)	Specificity (%)	Positive predictive value*
Peters, et al., 19961			
6.3 (2)	66	98	63
6.8 (3)	48	100	90
7.3 (4)	36	100	97
Rohlfing, et al., 20002			
5.6 (1)	83.4	84.4	25
6.1 (2)	63.2	97.4	57

6.5 (3)	42.8	99.6	86
7.0 (4)	28.3	99.9	94

*-Positive predictive values were calculated using an assumed diabetes prevalence rate of 6 percent in the general population (i.e., persons without known diabetes).

Information from references 1 and 2.

A subsequent study2 that used current WHO criteria for defining diabetes (i.e., fasting plasma glucose of 126 mg per dL [7.0 mmol per L] or more) showed similar results. This cross-sectional study3 of 6,559 patients that used a cutoff A1C level of 6.1 percent and assumed a diabetes prevalence rate of 6 percent showed A1C testing was 63.2 percent sensitive and 97.4 percent specific for diagnosing diabetes (PPV = 57 percent). A subgroup analysis2 of these results showed that the sensitivity of A1C testing was considerably higher in Mexican Americans and blacks (83.6 and 75.8 percent, respectively) compared with non-Hispanic whites (58.6 percent). The reason for these differences is unclear; however, these results may suggest physiologic variations among ethnic groups. If this is verified in future, larger studies, A1C testing may have a role in diagnosing diabetes in some patient populations.

Recommendations from Others

The American Diabetes Association (ADA) does not recommend A1C testing for the diagnosis of diabetes.3 Instead, it recommends fasting plasma glucose testing (126 mg per dL or more is diagnostic) as the test of choice because it is easier and faster to perform and less expensive than other screening tests. Table 23 includes the ADA criteria for diagnosing diabetes. Although the ADA guideline points out that A1C testing historically had not been standardized among laboratories, the test has become widely standardized in the United States since the guideline's publication.4 The European Diabetes Policy Group guideline5 also does not recommend A1C testing for diagnosing diabetes and recommends confirming the diagnosis in persons with elevated A1C levels using fasting plasma glucose testing (126 mg per dL or more is diagnostic).

table 2

American Diabetes Association Criteria for the Diagnosis of Diabetes Mellitus*
Diabetes mellitus can be diagnosed if at least one of the following clinical findings is present:
Symptoms of diabetes (e.g., polyuria, polydipsia, unexplained weight loss) plus casual† plasma glucose ≥ 200 mg per dL (11.1 mmol per L)
Fasting‡ plasma glucose ≥ 126 mg per dL (7.0 mmol per L)
Two-hour postload glucose ≥ 200 mg per dL according to an oral glucose tolerance test§

*-In the absence of unequivocal hyperglycemia, these criteria should be confirmed by

repeat testing on another day.

†-A casual glucose measurement is determined any time of day without regard to time since last meal.

‡-Fasting is defined as no caloric intake for at least eight hours.

§-Oral glucose tolerance tests are not recommended for routine clinical use and should be performed as described by the World Health Organization (i.e., using a glucose load containing the equivalent of 75 g of anhydrous glucose dissolved in water).

Adapted with permission from Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 2003;26(suppl 1):S12.

Clinical Commentary

Although most of the literature on diabetes includes the two-hour OGTT as the standard test for diagnosing diabetes, in daily clinical practice, this approach is not always feasible. Fasting plasma glucose testing has been shown to have slightly lower sensitivity for predicting microvascular complications from diabetes compared with the two-hour OGTT, but it is easier to perform compared with the two-hour OGTT. Therefore, fasting plasma glucose testing is widely used as the preferred diagnostic test.

Some physicians believe that because glycemic treatment for diabetes is not aggressively initiated until A1C levels are 7 percent or more, A1C testing can be used for diagnosis despite its low sensitivity. However, there are other important interventions (e.g., improving blood pressure, lowering low-density lipoprotein cholesterol, aspirin therapy, influenza vaccination) that are recommended for patients with diabetes, even those with A1C levels less than 7 percent.[6] Therefore, fasting plasma glucose testing remains the preferred diagnostic test for diabetes.

TAE JOON LEE, M.D.

East Carolina University Brody School of Medicine
Department of Family Medicine
Geriatrics Division
Greenville, North Carolina

SARAH SAFRANEK, M.L.I.S.

University of Washington Health Sciences Libraries
Seattle, Washington

Address correspondence by e-mail to Tae Joon Lee, M.D., at leetae@ecu.edu. Reprints are not available from the authors.

REFERENCES

1. Peters AL, Davidson MB, Schriger DL, Hasselblad V, for the Meta-analysis Research Group on the Diagnosis of Diabetes Using Glycated Hemoglobin Levels. A clinical approach for the diagnosis of diabetes mellitus: an analysis using glycosylated hemoglobin levels [Published correction appears in JAMA 1997;277:1125]. JAMA 1996;276:1246-52.

2. Rohlfing CL, Little RR, Wiedmeyer HM, England JD, Madsen R, Harris MI, et al. Use of GHb (HbA1c) in screening for undiagnosed diabetes in the U.S. population [Published correction appears in Diabetes Care 2000;23:876]. Diabetes Care 2000;23:187-91.

3. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 2003;26(suppl 1):S5-S20.

4. Kilpatrick E. Glycated haemoglobin in the year 2000. J Clin Pathol 2000;53:335-9.

5. European Diabetes Policy Group 1999. A desktop guide to type 2 diabetes mellitus. Diabet Med 1999;16:716-30.

6. American Diabetes Association. Standards of medical care in diabetes [Published correction appears in Diabetes Care 2005;28:990]. Diabetes Care 2005;28(suppl 1):S4-S36.

Clinical Inquiries provides answers to questions submitted by practicing family physicians to the Family Physicians Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendation and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group (http://www.cebm.net/levels_of_evidence.asp).

This series of Clinical Inquiries is coordinated for American Family Physician by John Epling, M.D., State University of New York Upstate Medical University, Syracuse, N.Y. The complete database of evidence-based questions and answers is copyrighted by FPIN. If you are interested in submitting questions to be answered or writing answers for this series, go to http://www.fpin.org or contact questions@fpin.org.

A collection of FPIN's Clinical Inquiries published in AFP is available at http://www.aafp.org/afp/fpin.